

(FILE 'HOME' ENTERED AT 10:55:29 ON 17 DEC 2003)

FILE 'USPATFULL, CAPLUS' ENTERED AT 10:55:48 ON 17 DEC 2003
ACTIVATE L09980406/L

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L1      STR
L2 (    11)SEA FILE=REGISTRY SSS FUL L1
L3 (    30)SEA FILE=CAPLUS ABB=ON  PLU=ON  L2
L4 (    14)SEA FILE=CAPLUS ABB=ON  PLU=ON  L2/USES OR L2/BIOL
L5 (      0)SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND HAIR
L6 (      0)SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND THYROIDR
L7 (    13)SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND THYROID
L8 (      0)SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND ALOPECIA
L9 (      0)SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND BALD?
L10 (     3)SEA FILE=USPATFULL ABB=ON  PLU=ON  L2
L11 (     2)SEA FILE=CAPLUS ABB=ON  PLU=ON  40487-99-8/BIOL
L12 (     0)SEA FILE=TOXCENTER ABB=ON  PLU=ON  40487-99-8/BIOL
L13 (     2)SEA 40487-99-8/BIOL
L14 (     2)SEA FILE=CAPLUS ABB=ON  PLU=ON  40487-99-8
L15 (     0)SEA FILE=TOXCENTER ABB=ON  PLU=ON  40487-99-8
L16 (     2)SEA 40487-99-8
L17 (     1)SEA FILE=CAPLUS ABB=ON  PLU=ON  27486-96-0
L18 (     0)SEA FILE=TOXCENTER ABB=ON  PLU=ON  27486-96-0
L19 (     1)SEA 27486-96-0
L20 (    12)SEA FILE=CAPLUS ABB=ON  PLU=ON  52050-08-5 OR 40487-99-8 OR L17
L21 (     1)SEA FILE=TOXCENTER ABB=ON  PLU=ON  52050-08-5 OR 40487-99-8 OR
L22 (    13)SEA 52050-08-5 OR 40487-99-8 OR L19
L23 (    10)SEA FILE=CAPLUS ABB=ON  PLU=ON  CARDIAC SPARING
L24 (     8)SEA FILE=USPATFULL ABB=ON  PLU=ON  CARDIAC SPARING
L25 (    18)SEA CARDIAC SPARING
L26 (    19)SEA FILE=CAPLUS ABB=ON  PLU=ON  CARDIAC (5A) SPARING
L27 (    35)SEA FILE=USPATFULL ABB=ON  PLU=ON  CARDIAC (5A) SPARING
L28 (    54)SEA CARDIAC (5A) SPARING
L29 (     4)SEA FILE=CAPLUS ABB=ON  PLU=ON  THYROID AND L26
L30 (     5)SEA FILE=USPATFULL ABB=ON  PLU=ON  THYROID AND L27
L31 (     9)SEA THYROID AND L28
L32 (     0)SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 AND L26
L33 (     0)SEA FILE=USPATFULL ABB=ON  PLU=ON  L22 AND L27
L34 (     0)SEA L22 AND L28
L35 (     0)SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 AND (CARDIAC)
L36 (     0)SEA FILE=USPATFULL ABB=ON  PLU=ON  L22 AND (CARDIAC)
L37 (     0)SEA L22 AND (CARDIAC)
L38 (     1)SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 AND (HEART OR PRESSURE)
L39 (     0)SEA FILE=USPATFULL ABB=ON  PLU=ON  L22 AND (HEART OR PRESSURE)
L40 (     1)SEA L22 AND (HEART OR PRESSURE)
L41 (     1)SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 AND (HEART OR PRESSURE)
L42 (     0)SEA FILE=TOXCENTER ABB=ON  PLU=ON  L21 AND (HEART OR PRESSURE)
L43 (     1)SEA L40
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FILE 'REGISTRY, USPATFULL, CAPLUS' ENTERED AT 10:56:17 ON 17 DEC 2003

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L44      1 FILE REGISTRY
L45      11 FILE REGISTRY
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FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:02:03 ON 17 DEC 2003

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L46      30 FILE CAPLUS
L47       3 FILE USPATFULL
L48       5 FILE TOXCENTER
TOTAL FOR ALL FILES
L49      38 S L45
L50       2 FILE CAPLUS
L51       0 FILE USPATFULL
L52       0 FILE TOXCENTER
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TOTAL FOR ALL FILES
 L53 2 S TRIMETHYLTHYRONINE
 L54 4 FILE CAPLUS
 L55 0 FILE USPATFULL
 L56 1 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L57 5 S TRIMETHYL(3A)THYRONINE
 L58 18002 FILE CAPLUS
 L59 3924 FILE USPATFULL
 L60 3208 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L61 25134 S (L-TYROSINE) OR (L(1W) TYROSINE)
 L62 47 FILE CAPLUS
 L63 33 FILE USPATFULL
 L64 6 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L65 86 S L61 (5A) (DIMETHYL)
 L66 100 FILE CAPLUS
 L67 104 FILE USPATFULL
 L68 9 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L69 213 S L61 (5A) (DIMETHYL?)
 L70 5 FILE CAPLUS
 L71 8 FILE USPATFULL
 L72 1 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L73 14 S L69 (5A) (HYDROXY?)
 L74 19717 FILE CAPLUS
 L75 2175 FILE USPATFULL
 L76 8512 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L77 30404 S 52050-08-5/RN OR ?THYRONINE? OR 52050-08-5
 L78 61 FILE CAPLUS
 L79 495 FILE USPATFULL
 L80 38 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L81 594 S L77 AND (HAIR? OR ALOPECIA OR BALD?)

 FILE 'REGISTRY' ENTERED AT 11:09:46 ON 17 DEC 2003
 L82 1 S THYRONINE/CN

 FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:10:13 ON 17 DEC 2003
 L83 8 FILE CAPLUS
 L84 436 FILE USPATFULL
 L85 3 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L86 447 S L81 AND (METHYL?)
 L87 9 FILE CAPLUS
 L88 428 FILE USPATFULL
 L89 5 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L90 442 S L81 AND (?METHYL)
 L91 10 FILE CAPLUS
 L92 445 FILE USPATFULL
 L93 7 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L94 462 S L86 OR L90

 FILE 'REGISTRY' ENTERED AT 11:17:55 ON 17 DEC 2003
 L95 1 S 6893-02-3/RN
 SET NOTICE 1 DISPLAY
 SET NOTICE LOGIN DISPLAY

 FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:19:00 ON 17 DEC 2003

L96 31768 FILE CAPLUS
 L97 58023 FILE USPATFULL
 L98 11948 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L99 101739 S TRIIODOTHYRONINE OR (L-T3) OR (L(1W) T3) OR T3 OR (TRIIODO (5
 L100 2550638 FILE CAPLUS
 L101 873754 FILE USPATFULL
 L102 497113 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L103 3921505 S SUBSTITUT? OR ALKYLAT? OR METHYL?
 L104 1344 FILE CAPLUS
 L105 1011 FILE USPATFULL
 L106 437 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L107 2792 S L99 (2S) (L103 OR (FREE (3A) IODINE))
 L108 1156 FILE CAPLUS
 L109 1010 FILE USPATFULL
 L110 348 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L111 2514 S L99 (1S) (L103 OR (FREE (3A) IODINE))
 L112 14 FILE CAPLUS
 L113 2 FILE USPATFULL
 L114 9 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L115 25 S L99 (1S) ((FREE (3A) IODINE))

FILE 'REGISTRY' ENTERED AT 11:28:03 ON 17 DEC 2003

FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:28:06 ON 17 DEC 2003

FILE 'REGISTRY' ENTERED AT 11:28:19 ON 17 DEC 2003

FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:28:20 ON 17 DEC 2003

FILE 'REGISTRY' ENTERED AT 11:28:26 ON 17 DEC 2003

FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:28:28 ON 17 DEC 2003

FILE 'REGISTRY' ENTERED AT 11:28:33 ON 17 DEC 2003

FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:28:35 ON 17 DEC 2003

FILE 'REGISTRY' ENTERED AT 11:28:41 ON 17 DEC 2003

FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:28:42 ON 17 DEC 2003

L116 2 FILE CAPLUS
 L117 1 FILE USPATFULL
 L118 0 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L119 3 S L99 (1S) ((FREE (3A) HALOGEN?))
 L120 2 FILE CAPLUS
 L121 1 FILE USPATFULL
 L122 0 FILE TOXCENTER
 TOTAL FOR ALL FILES
 L123 3 S L119 NOT L115

FILE 'USPATFULL, CAPLUS' ENTERED AT 11:40:44 ON 17 DEC 2003

L124 343 FILE USPATFULL
 L125 17177 FILE CAPLUS
 TOTAL FOR ALL FILES
 L126 17520 S 6893-02-3/RN OR 6893-02-3
 L127 58067 FILE USPATFULL
 L128 32491 FILE CAPLUS
 TOTAL FOR ALL FILES

L129 90558 S L99 OR L126
L130 3 FILE USPATFULL
L131 99 FILE CAPLUS
TOTAL FOR ALL FILES
L132 102 S L129 (2S) (FREE (5A) (HALOGEN OR IODO?))
L133 2 FILE USPATFULL
L134 99 FILE CAPLUS
TOTAL FOR ALL FILES
L135 101 S L132 NOT 119
L136 2 FILE USPATFULL
L137 98 FILE CAPLUS
TOTAL FOR ALL FILES
L138 100 S L135 NOT L115
SAVE ALL L09980406/L

FILE 'EMBASE, MEDLINE, BIOSIS, SCISEARCH' ENTERED AT 11:54:24 ON 17 DEC 2003

L139 30070 FILE EMBASE
L140 33763 FILE MEDLINE
L141 32585 FILE BIOSIS
L142 18104 FILE SCISEARCH
TOTAL FOR ALL FILES
L143 114522 S L129
L144 7 FILE EMBASE
L145 4 FILE MEDLINE
L146 4 FILE BIOSIS
L147 4 FILE SCISEARCH
TOTAL FOR ALL FILES
L148 19 S L143 (1S) ((ME OR METHYL OR ALKYL) (2W) SUBSTITUT?)
L149 11 DUP REM L148 (8 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 12:02:03 ON 17 DEC 2003
SAVE ALL L099804

L115 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

AB Iodide does not exchange with iodinated thyronines under conditions which assure the absence of **free iodine**. Iodine exchanges readily with both thyroxine and **triiodothyronine** in synthetic soln. at physiol. pH. The rate of exchange at $10^{-4}M$ far exceeds that of substitution under the same conditions. The distribution of radioactivity is proportional to the molar ratios of the products, i.e., quant. Labeling by exchange involves only the "prime" positions. A new solvent is described which provides excellent resolution of the compds. encountered; it is tert-AmOH satd. with 2N NH₄OH.

ACCESSION NUMBER: 1955:46576 CAPLUS
DOCUMENT NUMBER: 49:46576
ORIGINAL REFERENCE NO.: 49:9070a-c
TITLE: The exchange of iodine with thyroxine homologs
AUTHOR(S): Gleason, Geoffrey I.
CORPORATE SOURCE: Abbott Labs., Oak Ridge, TN
SOURCE: Journal of Biological Chemistry (1955), 213, 837-41
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

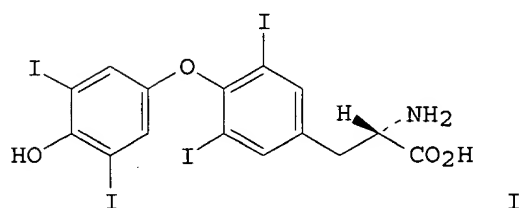
AN 72:133162 CA
 TI Thyroxine analogs. XVIII. 3,5-Dialkyl-3'-halo-DL-thyronines and their 3'-methyl and 4'-amino analogs
 AU Jorgensen, Eugene C.; Wright, Jeremy
 CS Sch. of Pharm., Univ. of California, San Francisco, CA, USA
 SO Journal of Medicinal Chemistry (1970), 13(3), 367-70
 CODEN: JMCMAR; ISSN: 0022-2623
 DT Journal
 LA English
 CC 34 (Synthesis of Amino Acids, Peptides, and Proteins)
 AB The synthesis of 3,5-diisopropyl- and 3,5-di-secbutyl-DL-thyronines and their 4'-amino, 3'-bromo, and 3'-iodo analogs is reported. 3,5-Diisopropyl-3'-methyl-DL-thyronine was also prepd. All 3,5-diisopropyl- and 3,5-di-sec-butyl-DL-thyronines and their derivs. and analogs were inactive as thyromimetics in the rat antigoiter test. The 3,5-dialkyl-3'-iodo-DL-thyronines of this series were also inactive as thyroxine-like agents by the heart-rate and tadpole metamorphosis methods. All analogs tested as thyroxine antagonists by the antigoiter assay were inactive.
 ST thyroxine analogs thyronines; thyronines thyroxine analogs
 IT Molecular structure-biological activity relationships (thyroxic, of thyronine alkyl derivs.)
 IT Thyronine, 3,5-dialkyl-3'-halo derivs., DL-Thyroxine, ar-alkyl analogs, DL-
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)
 IT 17944-26-2P 19288-25-6P 25806-78-4P 25849-86-9P 27144-21-4P
 27144-22-5P 27144-23-6P 27144-24-7P 27144-25-8P 27144-26-9P
 27144-27-0P 27144-28-1P 27144-29-2P 27192-12-7P 27192-13-8P
 27486-96-0P 27486-97-1P 27486-98-2P 27487-00-9P 27487-02-1P
 27487-03-2P
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

AN 72:133162 CA
 TI Thyroxine analogs. XVIII. 3,5-Dialkyl-3'-halo-DL-thyronines and their 3'-methyl and 4'-amino analogs
 AU Jorgensen, Eugene C.; Wright, Jeremy
 CS Sch. of Pharm., Univ. of California, San Francisco, CA, USA
 SO Journal of Medicinal Chemistry (1970), 13(3), 367-70
 CODEN: JMCMAR; ISSN: 0022-2623
 DT Journal
 LA English
 CC 34 (Synthesis of Amino Acids, Peptides, and Proteins)
 AB The synthesis of 3,5-diisopropyl- and 3,5-di-secbutyl-DL-thyronines and their 4'-amino, 3'-bromo, and 3'-iodo analogs is reported. 3,5-Diisopropyl-3'-methyl-DL-thyronine was also prepd. All 3,5-diisopropyl- and 3,5-di-sec-butyl-DL-thyronines and their derivs. and analogs were inactive as thyromimetics in the rat antigoiter test. The 3,5-dialkyl-3'-iodo-DL-thyronines of this series were also inactive as thyroxine-like agents by the heart-rate and tadpole metamorphosis methods. All analogs tested as thyroxine antagonists by the antigoiter assay were inactive.
 ST thyroxine analogs thyronines; thyronines thyroxine analogs
 IT Molecular structure-biological activity relationships (thyroxic, of thyronine alkyl derivs.)
 IT Thyronine, 3,5-dialkyl-3'-halo derivs., DL-Thyroxine, ar-alkyl analogs, DL-
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)
 IT 17944-26-2P 19288-25-6P 25806-78-4P 25849-86-9P 27144-21-4P
 27144-22-5P 27144-23-6P 27144-24-7P 27144-25-8P 27144-26-9P
 27144-27-0P 27144-28-1P 27144-29-2P 27192-12-7P 27192-13-8P
 27486-96-0P 27486-97-1P 27486-98-2P 27487-00-9P 27487-02-1P
 27487-03-2P
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

AN 72:133162 CA
TI Thyroxine analogs. XVIII. 3,5-Dialkyl-3'-halo-DL-thyronines and their
3'-methyl and 4'-amino analogs
AU Jorgensen, Eugene C.; Wright, Jeremy
CS Sch. of Pharm., Univ. of California, San Francisco, CA, USA
SO Journal of Medicinal Chemistry (1970), 13(3), 367-70
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
CC 34 (Synthesis of Amino Acids, Peptides, and Proteins)
AB The synthesis of 3,5-diisopropyl- and 3,5-di-secbutyl-DL-thyronines and
their 4'-amino, 3'-bromo, and 3'-iodo analogs is reported.
3,5-Diisopropyl-3'-methyl-DL-thyronine was also prepd. All
3,5-diisopropyl- and 3,5-di-sec-butyl-DL-thyronines and their derivs. and
analogues were inactive as thyromimetics in the rat antigoiter test. The
3,5-dialkyl-3'-iodo-DL-thyronines of this series were also inactive as
thyroxine-like agents by the heart-rate and tadpole metamorphosis methods.
All analogs tested as thyroxine antagonists by the antigoiter assay were
inactive.
ST thyroxine analogs thyronines; thyronines thyroxine analogs
IT Molecular structure-biological activity relationships
(thyroxic, of thyronine alkyl derivs.)

AN 78:154689 CA
TI Thyromimetic activity of 3,5,3'-trimethyl-L-thyronine
AU Jorgensen, Eugene C.; Block, Paul, Jr.
CS Sch. Ppharm., Univ. California, San Francisco, CA, USA
SO Journal of Medicinal Chemistry (1973), 16(3), 306-7
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
CC 1-3 (Pharmacodynamics)
Section cross-reference(s): 2
AB 3,5,3'-Trimethyl-L-thyronine (I) [40487-99-8] showed about 2% of the activity of L-thyroxine in reversing thiouracil-induced goiter in rats. I was thus the 1st reported nonhalogenated compd. having thyroid hormone activity. I was prepd. by the general method of P. Block Jr. and D. H. Coy (1972).
ST methylthyronine thyroid hormone activity; thyroxine analog synthesis
IT Thyroid hormones
RL: BIOL (Biological study)
(trimethylthyronine)
IT Goiter
(trimethylthyronine reversal of)
IT 40487-99-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thyromimetic activity of)

AN 87:16156 CA
 TI Thyroxine analogs. 23. Quantitative structure-activity correlation studies of in vivo and in vitro thyromimetic activities
 AU Dietrich, Stephen W.; Bolger, Michael B.; Kollman, Peter A.; Jorgensen, Eugene C.
 CS Sch. Pharm., Univ. California, San Francisco, CA, USA
 SO Journal of Medicinal Chemistry (1977), 20(7), 863-80
 CODEN: JMCMAR; ISSN: 0022-2623
 DT Journal
 LA English
 CC 2-3 (Hormone Pharmacology)
 Section cross-reference(s): 22, 34
 GI



AB Quant. structure-activity correlation studies of thyroxine (I) [51-48-9] and 78 analogs included studies of in vivo rat antgoiter activities, and in vitro binding affinities to intact rat hepatic nuclei, solubilized rat hepatic nuclear protein receptors, and plasma protein thyroxine-binding globulin, as well as correlation between in vivo and in vitro activities. Structure-activity relations including substituent effects such as steric effects, electron donation, H bonding, ionization, and lipophilicity, as well as free energy of binding are discussed.

ST thyroxine analog structure activity; thyroid hormone analog antgoiter; thyromimetic thyroxine analog; free energy binding thyroxine analog

IT Free energy
 (of binding, of thyroxine analogs to nuclear receptors, structure in relation to)

IT Substituent effect
 (on thyromimetic activity of thyroid hormone analogs)

IT Molecular structure-biological activity relationship
 (thyromimetic, of thyroid hormone analogs, calcn. of)

IT Thyroid hormones
 (thyroxine, quant. structure-activity relations of)

IT 4299-83-6 62901-40-0 62901-41-1 62901-42-2 62901-43-3 62901-44-4
 62901-45-5 62901-46-6 62901-47-7 62901-48-8 62901-51-3
 62960-49-0 67737-63-7
 RL: PROC (Process)
 (binding of, to hepatic nuclear protein receptors, free energy of)

IT 70-39-3 4080-15-3 4299-87-0 4564-77-6 5383-39-1 39693-06-6
 51725-31-6 58297-21-5 58297-22-6 62901-39-7
 RL: PROC (Process)
 (binding of, to hepatic nuclei, free energy of)

IT 51-48-9, biological studies 51-48-9D, analogs 534-51-0 3130-96-9
 3458-13-7 4080-14-2 10439-94-8
 RL: BIOL (Biological study)
 (thyromimetic activity of, calcn. of)

IT 4289-12-7 4299-83-6 4299-88-1 6893-08-9 6994-12-3 7582-57-2
 10468-95-8 17944-26-2 22153-98-6 25119-48-6 26384-19-0
 26384-20-3 26384-21-4 35152-70-6 35152-73-9 35152-79-5
 35152-81-9 37642-60-7 38896-90-1 40487-99-8 56807-75-1

60363-26-0	60497-68-9	61476-49-1	62901-23-9	62901-24-0
62901-25-1	62901-27-3	62901-28-4	62901-29-5	62901-30-8
62901-31-9	62901-32-0	62901-33-1	62901-34-2	62901-35-3
62901-36-4	62901-37-5	62901-38-6	62901-49-9	62901-50-2
62901-51-3	62901-52-4	62960-46-7	62960-48-9	62961-71-1
67737-63-7	91840-96-9			

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thyromimetic activity of, calcn. of)

AN 80:142047 CA
 TI Molecular orbital studies of thyroid hormone analogs
 AU Kollman, Peter A.; Murray, Wallace J.; Nuss, Merrill E.; Jorgensen, Eugene C.; Rothenberg, Steve
 CS Dep. Pharm. Chem., Univ. California, San Francisco, CA, USA
 SO Journal of the American Chemical Society (1973), 95(26), 8518
 CODEN: JACSAT; ISSN: 0002-7863
 DT Journal
 LA English
 CC 6-3 (General Biochemistry)
 Section cross-reference(s): 2
 AB Mol. orbital calcns. on thyroxine analogs indicate that the min. energy conformation for 3,5-disubstituted compds. is an important structural feature detg. biol. activity. The proximal conformation of 3,5,3'-triiodothyronine is predicted to be very slightly (0.2 kcal/mole) more stable than the distal. The representation of the valence electrons of Cl, Br, and I with 2s- and 2p-like at. orbitals appears to give a reasonably satisfactory representation of the electronic structure of these halogen compds.
 ST thyroid hormone analog conformation; thyroxine conformation; iodothyronine conformation
 IT Molecular structure-biological activity relationship
 (of thyroxine and triiodothyronine)
 IT Conformation and Conformers
 (of thyroxine and triiodothyronine analogs)
 IT Potential barrier
 (rotational, of thyroxine and triiodothyronine analogs)
 IT 1678-72-4 37642-60-7 52050-08-5
 RL: PRP (Properties)
 (conformation of, mol. orbital energy calcn. in, thyroid hormone activity in relation to)
 IT 51-48-9, properties 6893-02-3
 RL: PRP (Properties)
 (conformation of, mol. orbital energy calcns. in, biol. activity in relation to)
 IT 56-41-7, properties 60-18-4, properties
 RL: PRP (Properties)
 (mol. orbital energies of)
 IT 101-84-8 108-95-2, properties 123-31-9, properties 833-98-7
 22040-02-4 28419-69-4 51930-03-1 51930-04-2
 RL: PRP (Properties)
 (rotational energy of)

=> d 145 5 all

YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:y

AN 81:99798 CA
 TI Hormonally active halogen free analogs of thyroxine
 AU Jorgensen, E. C.; Frieden, E.; Block, P., Jr.
 CS Sch. Pharm., Univ. California, San Francisco, CA, USA
 SO Proceedings of the Western Pharmacology Society (1974), 17, 271-5
 CODEN: PWPSA8; ISSN: 0083-8969
 DT Journal
 LA English
 CC 2-3 (Hormone Pharmacology)
 AB Synthesis of thyroid hormone analogs which contained no halogens showed that neither the halogen atoms nor the ether oxygen were essential features for appreciable thyroid hormone activity. Nonpolar groups of limited size and shape, as substituents adjacent to the connecting bridge (3 and 5 positions), provide the steric constraint which defines this semirigid structure. Specific polar groups, an anionic sidechain (1-position) and phenolic hydroxyl group (4'-position, are required at opposite ends of the central core. Activity of this basal structure is enhanced by a lipophilic substituent adjacent to the phenolic group, and positioned distally in space to the nonphenolic ring. Since methylated analogs of thyroxine and triiodothyronine were active in the rat the concept of at least 2 active thyroid hormones was supported. The essential structure consisted of a central lipophilic core of 2 mutually perpendicular aromatic rings, insulated from each other and positioned at an angle of about 120.deg. by an appropriate bridging atom (O, C, or S).
 ST thyroid hormone analog structure activity
 IT Thyroid hormones
 RL: BIOL (Biological study)
 (analogs, biol. activity of, structure in relation to)
 IT Molecular structure-biological activity relationship
 (of thyroid hormone analogs)
 IT 2378-96-3 26384-44-1 30804-65-0 35897-89-3 37642-60-7 38896-90-1
 52050-08-5
 RL: BIOL (Biological study)
 (as thyroid hormone analog)
 IT 51-48-9, biological studies
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (biol. activity of)

AN 81:131122 CA
 TI Thyroxine analogs. 22. Thyromimetic activity of halogen-free derivatives of 3,5-dimethyl-L-thyronine
 AU Jorgensen, Eugene C.; Murray, Wallace J.; Block, Paul, Jr.
 CS Sch. Pharm., Univ. California, San Francisco, CA, USA
 SO Journal of Medicinal Chemistry (1974), 17(4), 434-9
 CODEN: JMCMAR; ISSN: 0022-2623
 DT Journal
 LA English
 CC 2-3 (Hormone Pharmacology)
 Section cross-reference(s): 34
 AB Of a series of 4 title compds. prepd. and tested in the rat antigoiter assay, 3,5-dimethyl-3'-isopropyl-L-thyronine (I) [26384-44-1] had 18% of the activity of L-thyroxine [51-48-9]. I was prepared from N-acetyl-3,5-diiodo-4-(4-methoxy-3-isopropylphenoxy)-L-phenylalanine Et ester [23241-32-9] by cyanation, hydrogenation, and HI cleavage of the methyl ether group. Activity in relation to replacement of halogen atoms on the thyronine nucleus by alkyl groups, and replacement of the central ether linkage by a methylene bridge is discussed. NMR and mass spectral data showed that compds. previously reported as 3,5,3',5'-tetramethyl-DL-thyronine [26384-21-4] and 3,5-dimethyl-3'-isopropyl-DL-thyronine [26384-20-3] were isomers of those structures.
 ST thyroxine alkyl analog goiter inhibitor; thyroid hormone alkyl thyronine
 IT Thyroid hormones
 RL: BIOL (Biological study)
 (halogen-free dimethylthyronine derivs.)
 IT Molecular structure-biological activity relationship
 (thyromimetic, of dimethylthyronine derivs.)
 IT 26384-21-4
 RL: BIOL (Biological study)
 (as structure for 3,5,3',5'-tetramethyl-DL-thyronine, NMR and mass spectrum in relation to)
 IT 26384-20-3
 RL: BIOL (Biological study)
 (as structure for 3,5-dimethyl-3'-isopropyl-DL-thyronine, NMR and mass spectrum in relation to)
 IT 23241-32-9
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (cyanation of)
 IT 35897-90-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (iodination of)
 IT 10024-90-5
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (oxidn. and hydrolysis of)
 IT 26384-44-1P 26384-50-9P 52050-08-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and thyromimetic activity of)
 IT 14786-82-4P 29358-99-4P 52498-34-7P 52498-35-8P 52498-36-9P
 52498-37-0P 52498-38-1P 52498-39-2P 52498-40-5P 52777-31-8P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of)
 IT 35897-89-3 37642-60-7
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (thyromimetic activity of)
 IT 51-48-9, biological studies
 RL: BIOL (Biological study)
 (thyromimetic activity of halogen-free dimethylthyronine derivs. in relation to)

AN 81:146096 CA
 TI Thyromimetic activity of methylthyronines in the bullfrog tadpole
 AU Frieden, Earl; Yoshizato, Katsutoshi
 CS Dep. Chem., Florida State Univ. , Tallahassee, FL, USA
 SO Endocrinology (1974), 95(1), 188-94
 CODEN: ENDOAO; ISSN: 0013-7227
 DT Journal
 LA English
 CC 2-4 (Hormone Pharmacology)
 Section cross-reference(s): 12
 AB On injection into bullfrog tadpole, 3'-isopropyl-3,5-dimethylthyronine (I) [26384-44-1] had 20-25% of the activity of L-thyroxine [51-48-9] when compared for effects on urea excretion and percent tail decrease. 3,5,3'-Trimethylthyronine [52050-08-5] and 3,5,3',5'-tetramethylthyronine [35897-89-3] showed .sim.15% of the activity of thyroxine. 3,5-Diiodo-4-(3',5'-diiodo-4'-hydroxybenzyl)-DL-phenyl acetic acid [38960-79-1] and 3,5-diiodo-4-(3'-iodo-4'-hydroxybenzyl)-DL-phenylalanine [37642-60-7] were equal to or slightly more active than the corresponding oxyether compd. The chem. structure required for a thyromimetic response consists of a central lipophilic core, sterically constrained by bulky 3,5,3'-substituents with 2 specific anionic groups, located at the distal ends of the mol. Apparently, neither the halogens nor the ether oxygen are essential features for significant thyroid hormone activity.
 ST methylthyronine thyroid hormone tadpole
 IT Thyroid hormones
 RL: BIOL (Biological study)
 (methylthyronine as)
 IT Molecular structure-biological activity relationship
 (thyromimetic, of methylthyronines)
 IT L-Tyrosine, O-(4-hydroxy-3,5-diiodophenyl)-3,5-diiodo-, analogs
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (thyromimetic activity of)
 IT 534-51-0 6893-02-3 26384-44-1 35897-89-3 35897-90-6 37642-60-7
 38960-79-1 52050-08-5
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (thyromimetic activity of)

AN 84:69625 CA

TI Binding of selected iodothyronine analogs to receptor sites of isolated rat hepatic nuclei. High correlation between structural requirements for nuclear binding and biological activity

AU Koerner, Diona; Schwartz, Harold L.; Surks, Martin I.; Oppenheimer, Jack H.; Jorgensen, Eugene C.

CS Dep. Med., Montefiore Hosp. Med. Cent., Bronx, NY, USA

SO Journal of Biological Chemistry (1975), 250(16), 6417-23
CODEN: JBCHA3; ISSN: 0021-9258

DT Journal

LA English

CC 2-1 (Hormone Pharmacology)

AB The limited capacity, high affinity binding of 35 iodothyronine analogues by rat liver nuclei was examd. in an in vitro system. The in vitro nuclear binding of all the analogues tested was highly correlated with their published thyromimetic potencies in the intact animals. Binding and biol. activity were greater for 3'-mono- than 3',5'-di-substituted iodothyronines. A 4'-hydroxyl group was essential, but the 3' substituent could be several halogen or nonhalogen groups for which the distal conformation was preferred. The ether linkage could be replaced equally well by a methylene or sulfur group. The presence of both 3 and 5 groups which were limited to halogens or small alkyl groups were necessary for the maintenance of significant activity. Halogen-free iodothyronines had very low, but significant activity both in vitro and in vivo. The data provide information on the structural requirements for thyroid hormone action and further support the physiol. relevance of the nuclear sites.

ST iodothyronine receptor liver nucleus; structure activity iodothyronine thyromimetic

IT Receptors
RL: BIOL (Biological study)
(for thyroid hormones, of liver nucleus)

IT Cell nucleus
(iodothyronine binding by, of liver)

IT Thyroid hormones
RL: BIOL (Biological study)
(receptor for, of liver nucleus)

IT Liver
(thyroid hormone receptor of nucleus of)

IT Molecular structure-biological activity relationship
(thyromimetic, of iodothyronine analogs)

IT 51-23-0 51-48-9, biological studies 70-40-6 857-98-7 1041-01-6
2378-96-3 3272-50-2 3272-52-4 3415-06-3 4080-15-3 4299-63-2
4299-64-3 4299-87-0 4564-77-6 5383-39-1 6893-02-3 10439-94-8
10466-20-3 13724-85-1 17944-26-2 25119-48-6 26384-44-1
28619-63-8 30804-62-7 30804-65-0 35897-89-3 37642-60-7
38896-90-1 39693-06-6 51725-31-6 52050-08-5 58297-21-5
58297-22-6 58297-23-7 58297-24-8
RL: BIOL (Biological study)
(thyromimetic activity of, liver nucleus binding in relation to)

(FILE 'HOME' ENTERED AT 10:55:29 ON 17 DEC 2003)

FILE 'USPATFULL, CAPLUS' ENTERED AT 10:55:48 ON 17 DEC 2003
ACTIVATE L09980406/L

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L1      STR
L2      (      11)SEA FILE=REGISTRY SSS FUL L1
L3      (      30)SEA FILE=CAPLUS ABB=ON  PLU=ON  L2
L4      (      14)SEA FILE=CAPLUS ABB=ON  PLU=ON  L2/USES OR L2/BIOL
L5      (          0)SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND HAIR
L6      (          0)SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND THYROIDR
L7      (      13)SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND THYROID
L8      (          0)SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND ALOPECIA
L9      (          0)SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND BALD?
L10     (          3)SEA FILE=USPATFULL ABB=ON  PLU=ON  L2
L11     (          2)SEA FILE=CAPLUS ABB=ON  PLU=ON  40487-99-8/BIOL
L12     (          0)SEA FILE=TOXCENTER ABB=ON  PLU=ON  40487-99-8/BIOL
L13     (          2)SEA 40487-99-8/BIOL
L14     (          2)SEA FILE=CAPLUS ABB=ON  PLU=ON  40487-99-8
L15     (          0)SEA FILE=TOXCENTER ABB=ON  PLU=ON  40487-99-8
L16     (          2)SEA 40487-99-8
L17     (          1)SEA FILE=CAPLUS ABB=ON  PLU=ON  27486-96-0
L18     (          0)SEA FILE=TOXCENTER ABB=ON  PLU=ON  27486-96-0
L19     (          1)SEA 27486-96-0
L20     (      12)SEA FILE=CAPLUS ABB=ON  PLU=ON  52050-08-5 OR 40487-99-8 OR L17
L21     (          1)SEA FILE=TOXCENTER ABB=ON  PLU=ON  52050-08-5 OR 40487-99-8 OR
L22     (      13)SEA 52050-08-5 OR 40487-99-8 OR L19
L23     (      10)SEA FILE=CAPLUS ABB=ON  PLU=ON  CARDIAC SPARING
L24     (          8)SEA FILE=USPATFULL ABB=ON  PLU=ON  CARDIAC SPARING
L25     (      18)SEA CARDIAC SPARING
L26     (      19)SEA FILE=CAPLUS ABB=ON  PLU=ON  CARDIAC (5A) SPARING
L27     (      35)SEA FILE=USPATFULL ABB=ON  PLU=ON  CARDIAC (5A) SPARING
L28     (      54)SEA CARDIAC (5A) SPARING
L29     (          4)SEA FILE=CAPLUS ABB=ON  PLU=ON  THYROID AND L26
L30     (          5)SEA FILE=USPATFULL ABB=ON  PLU=ON  THYROID AND L27
L31     (          9)SEA THYROID AND L28
L32     (          0)SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 AND L26
L33     (          0)SEA FILE=USPATFULL ABB=ON  PLU=ON  L22 AND L27
L34     (          0)SEA L22 AND L28
L35     (          0)SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 AND (CARDIAC)
L36     (          0)SEA FILE=USPATFULL ABB=ON  PLU=ON  L22 AND (CARDIAC)
L37     (          0)SEA L22 AND (CARDIAC)
L38     (          1)SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 AND (HEART OR PRESSURE)
L39     (          0)SEA FILE=USPATFULL ABB=ON  PLU=ON  L22 AND (HEART OR PRESSURE)
L40     (          1)SEA L22 AND (HEART OR PRESSURE)
L41     (          1)SEA FILE=CAPLUS ABB=ON  PLU=ON  L20 AND (HEART OR PRESSURE)
L42     (          0)SEA FILE=TOXCENTER ABB=ON  PLU=ON  L21 AND (HEART OR PRESSURE)
L43     (          1)SEA L40
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FILE 'REGISTRY, USPATFULL, CAPLUS' ENTERED AT 10:56:17 ON 17 DEC 2003

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L44      1 FILE REGISTRY
L45      11 FILE REGISTRY
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FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:02:03 ON 17 DEC 2003

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L46      30 FILE CAPLUS
L47      3 FILE USPATFULL
L48      5 FILE TOXCENTER
TOTAL FOR ALL FILES
L49      38 S L45
L50      2 FILE CAPLUS
L51      0 FILE USPATFULL
L52      0 FILE TOXCENTER
TOTAL FOR ALL FILES
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L53      2 S TRIMETHYLTHYRONINE
L54      4 FILE CAPLUS
L55      0 FILE USPATFULL
L56      1 FILE TOXCENTER
TOTAL FOR ALL FILES
L57      5 S TRIMETHYL(3A) THYRONINE
L58      18002 FILE CAPLUS
L59      3924 FILE USPATFULL
L60      3208 FILE TOXCENTER
TOTAL FOR ALL FILES
L61      25134 S (L-TYROSINE) OR (L(1W) TYROSINE)
L62      47 FILE CAPLUS
L63      33 FILE USPATFULL
L64      6 FILE TOXCENTER
TOTAL FOR ALL FILES
L65      86 S L61 (5A) (DIMETHYL)
L66      100 FILE CAPLUS
L67      104 FILE USPATFULL
L68      9 FILE TOXCENTER
TOTAL FOR ALL FILES
L69      213 S L61 (5A) (DIMETHYL?)
L70      5 FILE CAPLUS
L71      8 FILE USPATFULL
L72      1 FILE TOXCENTER
TOTAL FOR ALL FILES
L73      14 S L69 (5A) (HYDROXY?)
L74      19717 FILE CAPLUS
L75      2175 FILE USPATFULL
L76      8512 FILE TOXCENTER
TOTAL FOR ALL FILES
L77      30404 S 52050-08-5/RN OR ?THYRONINE? OR 52050-08-5
L78      61 FILE CAPLUS
L79      495 FILE USPATFULL
L80      38 FILE TOXCENTER
TOTAL FOR ALL FILES
L81      594 S L77 AND (HAIR? OR ALOPECIA OR BALD?)

FILE 'REGISTRY' ENTERED AT 11:09:46 ON 17 DEC 2003
L82      1 S THYRONINE/CN

FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:10:13 ON 17 DEC 2003
L83      8 FILE CAPLUS
L84      436 FILE USPATFULL
L85      3 FILE TOXCENTER
TOTAL FOR ALL FILES
L86      447 S L81 AND (METHYL?)
L87      9 FILE CAPLUS
L88      428 FILE USPATFULL
L89      5 FILE TOXCENTER
TOTAL FOR ALL FILES
L90      442 S L81 AND (?METHYL)
L91      10 FILE CAPLUS
L92      445 FILE USPATFULL
L93      7 FILE TOXCENTER
TOTAL FOR ALL FILES
L94      462 S L86 OR L90

FILE 'REGISTRY' ENTERED AT 11:17:55 ON 17 DEC 2003
L95      1 S 6893-02-3/RN
          SET NOTICE 1 DISPLAY
          SET NOTICE LOGIN DISPLAY

FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:19:00 ON 17 DEC 2003
L96      31768 FILE CAPLUS

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L97      58023 FILE USPATFULL
L98      11948 FILE TOXCENTER
TOTAL FOR ALL FILES
L99      101739 S TRIIODOTHYRONINE OR (L-T3) OR (L(1W) T3) OR T3 OR (TRIIODO (5
L100     2550638 FILE CAPLUS
L101     873754 FILE USPATFULL
L102     497113 FILE TOXCENTER
TOTAL FOR ALL FILES
L103     3921505 S SUBSTITUT? OR ALKYLAT? OR METHYL?
L104     1344 FILE CAPLUS
L105     1011 FILE USPATFULL
L106     437 FILE TOXCENTER
TOTAL FOR ALL FILES
L107     2792 S L99 (2S) (L103 OR (FREE (3A) IODINE))
L108     1156 FILE CAPLUS
L109     1010 FILE USPATFULL
L110     348 FILE TOXCENTER
TOTAL FOR ALL FILES
L111     2514 S L99 (1S) (L103 OR (FREE (3A) IODINE))
L112     14 FILE CAPLUS
L113     2 FILE USPATFULL
L114     9 FILE TOXCENTER
TOTAL FOR ALL FILES
L115     25 S L99 (1S) ((FREE (3A) IODINE))

FILE 'REGISTRY' ENTERED AT 11:28:03 ON 17 DEC 2003

FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:28:06 ON 17 DEC 2003

FILE 'REGISTRY' ENTERED AT 11:28:19 ON 17 DEC 2003

FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:28:20 ON 17 DEC 2003

FILE 'REGISTRY' ENTERED AT 11:28:26 ON 17 DEC 2003

FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:28:28 ON 17 DEC 2003

FILE 'REGISTRY' ENTERED AT 11:28:33 ON 17 DEC 2003

FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:28:35 ON 17 DEC 2003

FILE 'REGISTRY' ENTERED AT 11:28:41 ON 17 DEC 2003

FILE 'CAPLUS, USPATFULL, TOXCENTER' ENTERED AT 11:28:42 ON 17 DEC 2003
L116     2 FILE CAPLUS
L117     1 FILE USPATFULL
L118     0 FILE TOXCENTER
TOTAL FOR ALL FILES
L119     3 S L99 (1S) ((FREE (3A) HALOGEN?))
L120     2 FILE CAPLUS
L121     1 FILE USPATFULL
L122     0 FILE TOXCENTER
TOTAL FOR ALL FILES
L123     3 S L119 NOT L115

FILE 'USPATFULL, CAPLUS' ENTERED AT 11:40:44 ON 17 DEC 2003
L124     343 FILE USPATFULL
L125     17177 FILE CAPLUS
TOTAL FOR ALL FILES
L126     17520 S 6893-02-3/RN OR 6893-02-3
L127     58067 FILE USPATFULL
L128     32491 FILE CAPLUS
TOTAL FOR ALL FILES
L129     90558 S L99 OR L126

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L130 3 FILE USPATFULL
L131 99 FILE CAPLUS
TOTAL FOR ALL FILES
L132 102 S L129 (2S) (FREE (5A) (HALOGEN OR IODO?))
L133 2 FILE USPATFULL
L134 99 FILE CAPLUS
TOTAL FOR ALL FILES
L135 101 S L132 NOT 119
L136 2 FILE USPATFULL
L137 98 FILE CAPLUS
TOTAL FOR ALL FILES
L138 100 S L135 NOT L115
 SAVE ALL L09980406/L

L149 ANSWER 8 OF 11 MEDLINE on STN
AN 60055782 MEDLINE
DN 60055782
TI Effects of **methyl** group **substitution** for iodine on
metabolic activity of thyroxine, **triiodothyronine** and
tetraiodothyropropionic acid.
AU PITTMAN C S; SHIDA H; BARKER S B
SO Endocrinology, (1961 Feb) 68 248-52.
DT Journal
LA English
FS OLDMEDLINE
EM 196112
ED Entered STN: 19990716
Last Updated on STN: 19990716
ST basal metabolism - pharmacology; thyroxin - related compounds; tissue
metabolism - pharmacology; triiodothyronine - related compounds
RN 51-48-9 (THYROXIN); 6893-02-3 (TRIIODOTHYRONINE)

L149 ANSWER 2 OF 11 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 2

AN 95198257 EMBASE

DN 1995198257

TI Synthesis and structure-activity relationships of oxamic acid and acetic acid derivatives related to L-thyronine.

AU Yokoyama N.; Walker G.N.; Main A.J.; Stanton J.L.; Morrissey M.M.; Boehm C.; Engle A.; Neubert A.D.; Wasvary J.M.; Stephan Z.F.; Steele R.E.

CS Research Department, Ciba Pharmaceuticals, 556 Morris Avenue, Summit, NJ 07901, United States

SO Journal of Medicinal Chemistry, (1995) 38/4 (695-707).

ISSN: 0022-2623 CODEN: JMCMAR

CY United States

DT Journal; Article

FS 030 Pharmacology

037 Drug Literature Index

LA English

SL English

AB Aryloxamic acids 7 and 23, (arylamino)acetic acids 29, arylpropionic acids 33, arylthioacetic acids 37, and (aryloxy)acetic acid 41 related to L-triiodothyronine (L-T3) were prepared and tested in vitro for binding to the rat liver nuclear L-T3 receptor and the rat membrane L-T3 receptor. The structure-activity relationships for these compounds are described, with 7f, 23a, 29c, 33a, 37b, and 41 showing excellent potency (IC50's of 0.19, 0.16, 1.1, 0.11, 3.5, and 0.10 nM, respectively) to the nuclear receptor and significantly lower binding affinity to the membrane receptor (IC50's > 5 .mu.M). Some of these compounds, especially in the oxamic acid series 7 and 23, showed an unprecedented potency for methyl-substituted derivatives such as 7f and 23a. Compounds 7f and 23a showed good lipid lowering effects in rats with ED50's of 20 and 5 .mu.g/kg po, respectively, and a lack of cardiac side effects in rats at doses as high as 10 and 25 mg/kg po, respectively.

CT Medical Descriptors:

animal cell

animal model

animal tissue

article

binding affinity

cardiotoxicity

controlled study

dose response

drug potency

drug synthesis

lipid blood level

male

nonhuman

oral drug administration

rat

structure activity relation

Drug Descriptors:

*liothyronine receptor

cell nucleus receptor

membrane receptor

*3,5 dibromo 3' (2,3 dihydro 3 oxo 6 pyridazinylmethyl)thyronine: PD, pharmacology

*3,5 dibromo 3' (2,3 dihydro 3 oxo 6 pyridazinylmethyl)thyronine: AN, drug analysis

*3,5 dibromo 3' (2,3 dihydro 3 oxo 6 pyridazinylmethyl)thyronine: CM, drug comparison

*3,5 dibromo 3' (2,3 dihydro 3 oxo 6 pyridazinylmethyl)thyronine: DV, drug development

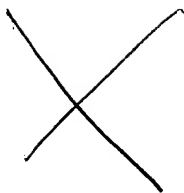
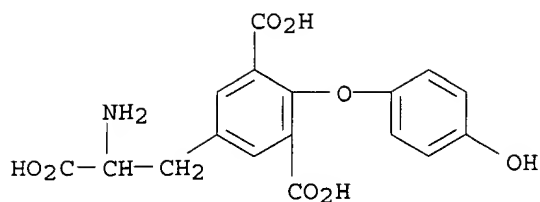
*hypocholesterolemic agent: PD, pharmacology

*hypocholesterolemic agent: DV, drug development
 *hypocholesterolemic agent: CM, drug comparison
 *hypocholesterolemic agent: AN, drug analysis
 *liothyronine: PD, pharmacology
 [[4 [3 (4 fluoro alpha hydroxybenzyl) 4 hydroxyphenoxy] 3,5
 dimethylphenyl]amino]oxoacetic acid ethyl ester: CM, drug comparison
 [[4 [3 (4 fluoro alpha hydroxybenzyl) 4 hydroxyphenoxy] 3,5
 dimethylphenyl]amino]oxoacetic acid ethyl ester: AN, drug analysis
 [[4 [3 (4 fluoro alpha hydroxybenzyl) 4 hydroxyphenoxy] 3,5
 dimethylphenyl]amino]oxoacetic acid ethyl ester: PD, pharmacology
 [[4 [3 (4 fluoro alpha hydroxybenzyl) 4 hydroxyphenoxy] 3,5
 dimethylphenyl]amino]oxoacetic acid ethyl ester: DV, drug development
 cholesterol: EC, endogenous compound
 n [3,5 dimethyl 4 (4 hydroxy 3 isopropylphenoxy)phenyl]oxamic acid: AN,
 drug analysis
 n [3,5 dimethyl 4 (4 hydroxy 3 isopropylphenoxy)phenyl]oxamic acid: CM,
 drug comparison
 n [3,5 dimethyl 4 (4 hydroxy 3 isopropylphenoxy)phenyl]oxamic acid: DV,
 drug development
 n [3,5 dimethyl 4 (4 hydroxy 3 isopropylphenoxy)phenyl]oxamic acid: PD,
 pharmacology
 unclassified drug
 RN (3,5 dibromo 3' (2,3 dihydro 3 oxo 6 pyridazinylmethyl)thyronine)
 105211-23-2; (liothyronine) 6138-47-2, 6893-02-3; (cholesterol) 57-88-5
 CN (1) L 94901
 CO (1) Smith kline and french

L123 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN

AB The mol. conformation of the **halogen-free** thyroid hormone analog, N-acetyl-4'-methoxy-3,5,3'-trimethyl-L-thyronine Et ester, was detd. by x-ray diffraction techniques. The obsd. mol. conformation was similar to that found for the natural hormone 3,5,3'-**triiodo-L-thyronine** (**T3**). In this structure, the 3'-Me group is distal, the overall conformation is cisoid, and the di-Ph ether conformation is twist-skewed. These structural similarities with **T3** showed that the conformational features required by the active hormone can still be maintained with Me substitution. The observation that the **halogen-free** analogs have relatively high activity but extremely low protein binding affinity implies that the role of I in hormone transport and biol. activity can be differentiated. These data suggest that the I atoms enhance hormone-protein binding by virtue of their electronic, as well as steric, properties.

ACCESSION NUMBER: 1980:193090 CAPLUS
DOCUMENT NUMBER: 92:193090
TITLE: Role of iodine in thyroid hormones: molecular conformation of a halogen-free hormone analog
AUTHOR(S): Cody, Vivian
CORPORATE SOURCE: Med. Found. Buffalo, Inc., Buffalo, NY, 14203, USA
SOURCE: Journal of Medicinal Chemistry (1980), 23(5), 584-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

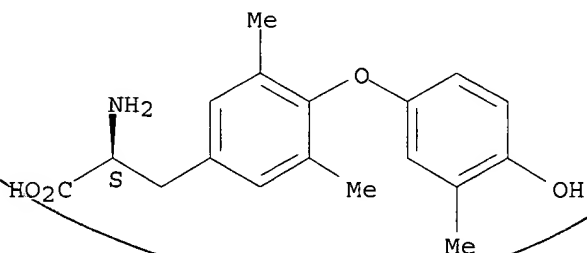


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L45- ANSWER 4 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 52050-08-5 REGISTRY
CN L-Tyrosine, O-(4-hydroxy-3-methylphenyl)-3,5-dimethyl- (9CI) (CA INDEX
NAME)
OTHER NAMES:
CN 3,5,3'-Trimethyl-L-thyronine
CN 3,5,3'-Trimethylthyronine
CN L-3,5,3'-Trimethylthyronine
FS STEREOSEARCH
MF C18 H21 N O4
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)

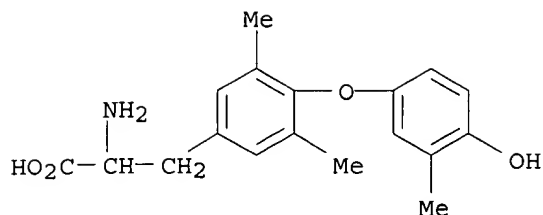
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1907 TO DATE)
9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L45- ANSWER 5 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 40487-99-8 REGISTRY
CN Tyrosine, O-(4-hydroxy-3-methylphenyl)-3,5-dimethyl- (9CI) (CA INDEX
NAME)
OTHER NAMES:
CN 3,5,3'-Trimethylthyronine
FS 3D CONCORD
DR 62960-43-4
MF C18 H21 N O4
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

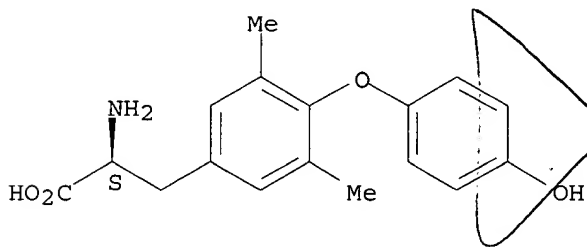


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L45 ANSWER 6 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 35897-90-6 REGISTRY
CN L-Tyrosine, O-(4-hydroxyphenyl)-3,5-dimethyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Alanine, 3-[4-(p-hydroxyphenoxy)-3,5-xylyl]- (7CI)
OTHER NAMES:
CN 3,5-Dimethyl-L-thyronine
CN L-3,5-Dimethylthyronine
FS STEREOSEARCH
MF C17 H19 N O4
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS
(*File contains numerically searchable property data)

Absolute stereochemistry.

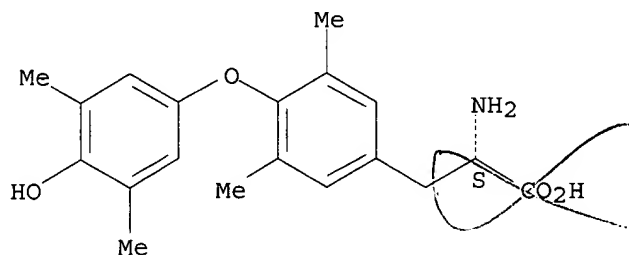


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L45 ANSWER 7 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 35897-89-3 REGISTRY
CN L-Tyrosine, O-(4-hydroxy-3,5-dimethylphenyl)-3,5-dimethyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3,5,3',5'-Tetramethyl-L-thyronine
CN 3,5,3',5'-Tetramethylthyronine
FS STEREOSEARCH
MF C19 H23 N O4
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

14 REFERENCES IN FILE CA (1907 TO DATE)

14 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L45 ANSWER 8 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN

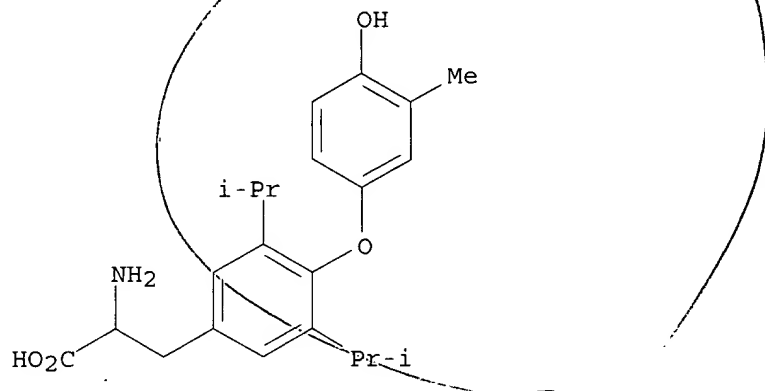
RN 27486-96-0 REGISTRY

CN Alanine, 3-[4-[(4-hydroxy-m-tolyl)oxy]-3,5-diisopropylphenyl]-, DL- (8CI)
(CA INDEX NAME)

MF C22 H29 N O4

LC STN Files: BEILSTEIN*, CA, CAPLUS

(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L45 ANSWER 9 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN

RN 26384-21-4 REGISTRY

CN Tyrosine, O-(4-hydroxy-3,5-dimethylphenyl)-3,5-dimethyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Alanine, 3-[4-[(4-hydroxy-3,5-xylyl)oxy]-3,5-xylyl]- (6CI, 7CI)

CN Alanine, 3-[4-[(4-hydroxy-3,5-xylyl)oxy]-3,5-xylyl]-, DL- (8CI)

CN DL-Tyrosine, O-(4-hydroxy-3,5-dimethylphenyl)-3,5-dimethyl-

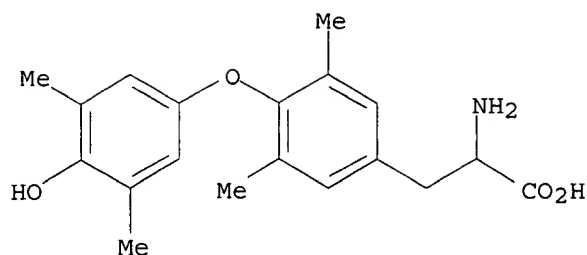
OTHER NAMES:

CN 3,5,3',5'-Tetramethyl-DL-thyronine

MF C19 H23 N O4

LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXCENTER

(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

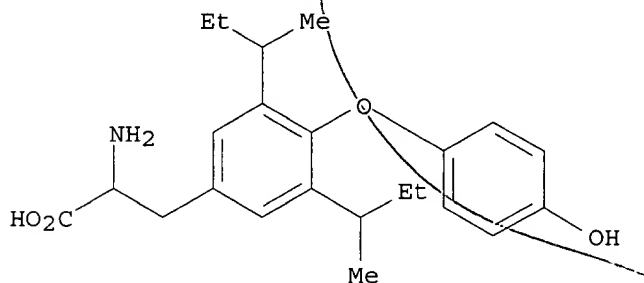
7 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)
4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L45 ANSWER 10 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 25849-86-9 REGISTRY
CN Tyrosine, O-(4-hydroxyphenyl)-3,5-bis(1-methylpropyl)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Alanine, 3-[3,5-di-sec-butyl-4-(p-hydroxyphenoxy)phenyl]-, DL- (8CI)
CN DL-Tyrosine, O-(4-hydroxyphenyl)-3,5-bis(1-methylpropyl)-
FS STEREOSEARCH
DR 25807-10-7
MF C23 H31 N O4
LC STN Files: ~~BEILSTEIN*, CA, CAPLUS~~

(*File contains numerically searchable property data)



458 10.1

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

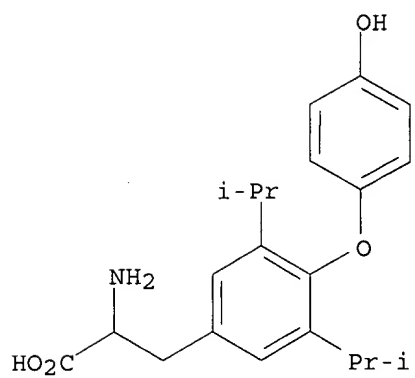
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L45 ANSWER 11 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 19288-25-6 REGISTRY
CN Tyrosine, O-(4-hydroxyphenyl)-3,5-bis(1-methylethyl)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Alanine, 3-[4-(p-hydroxyphenoxy)-3,5-diisopropylphenyl]-, DL- (8CI)
CN DL-Tyrosine, O-(4-hydroxyphenyl)-3,5-bis(1-methylethyl)-
DR 25807-09-4
MF C21 H27 N O4
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT

(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

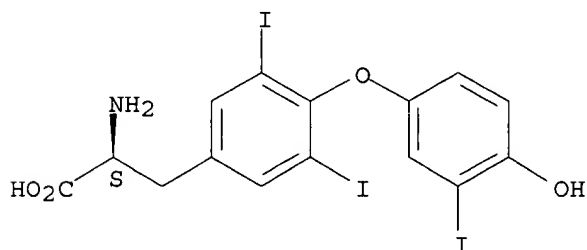
3 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=>

L95 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
 RN 6893-02-3 REGISTRY
 CN L-Tyrosine, O-(4-hydroxy-3-iodophenyl)-3,5-diiodo- (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN Alanine, 3-[4-(4-hydroxy-3-iodophenoxy)-3,5-diiodophenyl]-, L- (8CI)
 CN Thyronine, 3,3',5-triiodo-, L- (6CI)
 OTHER NAMES:
 CN 3,3',5-Triiodo-L-thyronine
 CN 3,3',5-Triiodothyronine
 CN 3,5,3'-Triiodothyronine
 CN 4-(4-Hydroxy-3-iodophenoxy)-3,5-diiodophenylalanine
 CN L-3,3',5-Triiodothyronine
 CN L-Liothyronine
 CN L-T3
 CN L-Triiodothyronine
 CN Liothyronin
 CN Liothyronine
 CN NSC 80203
 CN T3
 CN T3 (amino acid)
 CN T3 (Hormone)
 CN Tresitope
 CN Triiodo-L-thyronine
 CN Triiodothyronine
 FS STEREOSEARCH
 DR 7013-53-8, 57164-27-9
 MF C15 H12 I3 N O4
 CI COM
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSChem, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCoSEARCH, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
 (*File contains numerically searchable property data)
 Other Sources: EINECS**, WHO
 (**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (+).

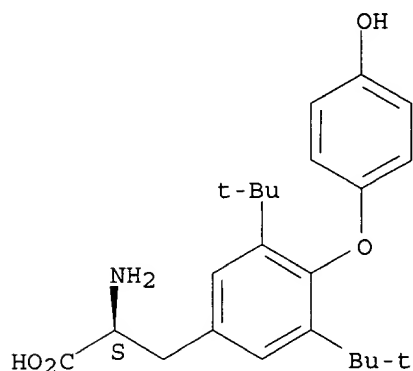


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

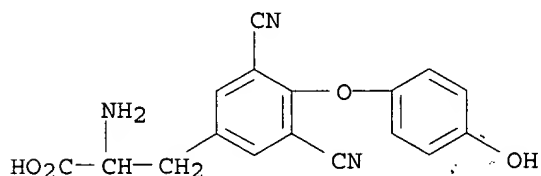
17162 REFERENCES IN FILE CA (1907 TO DATE)
 143 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 17176 REFERENCES IN FILE CAPLUS (1907 TO DATE)
 21 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L45 ANSWER 1 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
 RN 439573-89-4 REGISTRY
 CN L-Tyrosine, 3,5-bis(1,1-dimethylethyl)-O-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C23 H31 N O4
 SR Reaction Database
 LC STN Files: CASREACT

Absolute stereochemistry.



L45 ANSWER 2 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
 RN 93326-20-6 REGISTRY
 CN Alanine, 3-[3,5-dicyano-4-(p-hydroxyphenoxy)phenyl]- (7CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C17 H13 N3 O4
 LC STN Files: BEILSTEIN*, CAOLD
 (*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L45 ANSWER 3 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
 RN 93317-08-9 REGISTRY
 CN Isophthalic acid, 5-(2-amino-2-carboxyethyl)-2-(p-hydroxyphenoxy)- (7CI)
 (CA INDEX NAME)
 FS 3D CONCORD
 MF C17 H15 N O8
 LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS
 (*File contains numerically searchable property data)